

CLAIMS

What is claimed is:

1. A process for producing a SMAD interacting protein comprising:
conducting a two-hybrid screening assay wherein SMAD C-domain fused to a DNA-binding domain is used as bait and a vertebrate cDNA library is used as prey.
2. SMAD interacting protein produced by the process of claim 1.
3. A SMAD interacting protein of the family of zinc finger/homeodomain proteins including d-crystallin enhancer binding protein and/or *Drosophila* zfh-1, wherein said SMAD interacting protein:
does not interact with full size XSMAD1 in yeast,
 $SIP1_{czf}$ binds to E2 box sites,
 $SIP1_{czf}$ binds to the Brachyury protein binding site,
interferes with Brachyury-mediated transcription activation in cells, and
interacts with C-domain of SMAD 1, 2 and/or 5.
4. An isolated nucleic acid sequence comprising the nucleotide sequence as provided in SEQ ID NO: 1 coding for a SMAD interacting protein or a functional fragment thereof.
5. A recombinant expression vector comprising the isolated nucleic acid sequence of claim 4 operably linked to a suitable control sequence.
6. A cell transfected or transduced with the recombinant expression vector of claim 5.
7. A nucleic acid sequence hybridizing to the nucleotide sequence as provided in SEQ ID NO: 1, or part thereof, and encoding a SMAD interacting protein or a functional fragment thereof.

- PCT/US2007/063533
8. A polypeptide comprising the amino acid sequence of SEQ ID NO: 2 or a functional fragment thereof.
 9. A pharmaceutical composition comprising the nucleic acid sequence of claim 4 or a nucleic acid that hybridizes to said sequence.
 10. A pharmaceutical composition comprising the polypeptide of claim 7, together with a suitable carrier.
 11. A method for diagnosing a disease in a subject, said disease selected from the group of diseases consisting of cancer, malformation, immune disease, neural disease, and bone metabolism disorders, said method comprising:
using the nucleic acid sequence of claim 4 or a nucleic acid that hybridizes to said sequence to analyze a sample taken from said subject.
 12. A method for diagnosing a disease in a subject, said disease selected from the group of diseases consisting of cancer, malformation, immune disease, neural disease, and bone metabolism disorders, said method comprising:
detecting the presence or absence of the polypeptide of claim 7 in a sample taken from said subject.
 13. A method of screening for compounds which affect the interaction between SMAD and SMAD interacting protein, comprising:
 14. A kit for diagnosing a disease selected from the group of diseases consisting of cancer, malformation, immune disease, neural disease, and bone metabolism, said kit comprising:
a first reactive component, said reactive component selected from the group consisting of
(A) an isolated nucleic acid sequence comprising the nucleotide sequence SEQ ID NO: 1 or a functional fragment thereof,

- (B) a nucleic acid sequence hybridizing to the nucleotide sequence of SEQ ID NO: 1, or part thereof, and encoding a SMAD interacting protein or a functional fragment thereof; and
- (C) a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 or a functional fragment thereof; and
- a second reactive component, reactive with the first reactive component in a detectable manner.
15. A transgenic animal harbouring the nucleic acid sequence of claim 4 or a nucleic acid that hybridizes to said sequence in its genome.
16. An improvement in a method of testing medicaments and therapy models in a test animal, the improvement comprising:
using the transgenic animal of claim 15 as the test animal in said method.
17. An isolated nucleic acid sequence comprising the nucleotide sequence of SEQ ID NO: 3 or a functional fragment thereof.
18. A polypeptide comprising the amino acid sequence of SEQ ID NO: 4 or a functional fragment thereof.
19. An isolated nucleic acid sequence comprising the nucleotide sequence as provided in SEQ ID NO: 8 or a functional fragment thereof.
20. Isolated nucleic acid sequence comprising the nucleotide sequence of SEQ ID NO: 10 coding for a SMAD interacting protein or a functional fragment thereof.

21. A polypeptide comprising the amino acid sequence depicted as the one letter code QHLGVGMEAPLLGFPTMNSNLSEVQKVLQIVDNTVSRQKMDCKTEDISKLK (SEQ ID NO: 21) necessary for binding with SMAD.
 22. A SMAD interacting protein of a family of proteins which contain a cluster of 5 CCCH-type zinc fingers including *Drosophila* “Clipper” and Zebrafish “No arches” wherein said SMAD interacting protein
 - interacts with full size XSMAD1 in yeast,
 - binds single or double stranded DNA,
 - has an RNase activity, and
 - interacts with C-domain of SMAD1, 2 and/or 5.
 23. A method for post-transcriptional regulation of gene expression by members of the TGF- β superfamily by manipulating or modulating the interaction between SMAD function and/or SMAD activity and mRNA stability.